Clean version of all pending claims

1. A method of screening two-compound or higher order combinations for biological activity using at least seven compounds in at least a seven-by-seven combinational array comprising at least forty-nine unique combinations of compounds, said method comprising the steps of:

(a) providing said compounds,

(b) creating said array of combinations of compounds,

(c) providing living test,

(d) contacting said array of combinations of compounds with said test cells under conditions that ensure that each compound combination/test cell contacting is segregated from the others,

(e) detecting or measuring a property of the test cells, and

(f) selecting combinations of compounds that cause an effect on said property of the test cells that is different from the effect of each compound of the combination by itself.

2. The method of claim 1, wherein steps (b) and (d) comprise sequentially contacting said compounds with said test cells, thereby creating said array in the presence of said test cells.

5. The method of claim 1, wherein said detecting step (e) is performed by a cytoblot assay.

6. The method of claim 1, wherein said detecting step (e) is performed by a reporter gene assay.

7. The method of claim 1, wherein said detecting step (e) is performed by a fluorescence resonance energy transfer assay.

8. The method of claim 1, wherein said detecting step (e) is performed by detecting a fluorescent calcium-binding indicator dye.

9. The method of claim 1, wherein said detecting step (e) employs fluorescence microscopy.

10. The method of claim 1, wherein step (e) employs expression profiling.

11. The method of claim 1, wherein said cells are human cells.

12. The method of claim 1, wherein said cells are selected from the group consisting of cancer cells, immune cells, neurons, and fibroblasts.

14. The method of claim 1, wherein one or both of steps (b) and (d) is carried out using a robotics system.

15. The method of claim 1, wherein one or both of steps (b) and (d) is carried out using microfluidics.

16. The method of claim 1, wherein one or both of steps (b) and (d) is carried out using ink-jet printer technology.

18. The method of claim 1, wherein said compounds are selected from the group consisting of non-polymeric organic compounds, lipids, carbohydrates, peptides, inorganic compounds, and oligonucleotides.

20. The method of claim 1, wherein at least one of said compounds is employed in purified form.

21. The method of claim 20, wherein each of said compounds is employed in purified form.

22. The method of claim 1, wherein said compounds are provided as components of mixtures.

23. The method of claim 22, wherein said mixtures are natural product extracts.

24. The method of claim 1, wherein said effect is a synergistic effect.

28. A method for screening two-compound or higher order combinations for biological activity, said method comprising the steps of:

(a) creating an array of at least 200 unique two-compound or higher order combinations from a set of compounds,

(b) providing living test cells,

(c) contacting said array of combinations of compounds with said test cells under conditions that ensure that each compound combination/test cell contacting is segregated from the others,

(d) detecting or measuring a property of the test cells, and

(e) selecting combinations of compounds that cause an effect on said property of the test cells that is different from the effect of each compound of the combination by itself.

29. The method of claim 28, wherein steps (a) – (c) comprise sequentially contacting said compounds with said test cells, thereby creating said array in the presence of said test cells.

30. The method of claim 28, further comprising the step of (f) repeating step (a) through (e) at least twice, wherein, in step (a), said array of at least 200 combinations is different in each repetition.

31. The method of claim 30, wherein at least two repetitions of step (f) occur within 10 days of each other.

32. The method of claim 28, wherein said array comprises at least 400 unique combinations.

33. The method of claim 28, wherein said array comprises at least 1540 unique combinations.

35. The method of claim 28, wherein said compounds are selected from the group consisting of non-polymeric organic compounds, lipids, carbohydrates, peptides, inorganic compounds, and oligonucleotides.

37. The method of claim 28, wherein at least one of said compounds is employed in purified form.

38. The method of claim 28, wherein each of said compounds is employed in purified form.

39. The method of claim 28, wherein said compounds are provided as components of mixtures.

40. The method of claim 39, wherein said mixtures are natural product extracts.

41. The method of claim 28, wherein said effect is a synergistic effect.

42. The method of claim 28, wherein one or both of steps (a) and (c) is carried out using a robotics system.

43. The method of claim 28, wherein one or both of steps (a) and (c) is carried out using microfluidics.

44. The method of claim 28, wherein one or both of steps (a) and (c) is carried out using ink-jet printer technology.

48. A method for screening two-compound or higher order combinations for biological activity, said method comprising the steps of:

(a) creating an array of at least 49 unique two-compound or higher order combinations,

(b) providing living test cells,

(c) contacting said array of combinations of compounds with said test cells under conditions that ensure that each compound combination/test cell contacting is segregated from the others,

(d) detecting or measuring a property of the test cells,

(e) selecting combinations of compounds that cause an effect on said property of the test cells that is different from the effect of each compound of the combination by itself, and

(f) repeating steps (a) through (e) at least 25 times over a one-week period, using a different array in each repetition.

49. The method of claim 48, wherein steps (a) through (e) are repeated at least 100 times over a 30-day period, using a different array in each repetition.

51. The method of claim 48, wherein said compounds are selected from the group consisting of non-polymeric organic compounds, lipids, carbohydrates, peptides, inorganic compounds, and oligonucleotides.

53. The method of claim 48, wherein said compounds are employed in purified form.

54. The method of claim 48, wherein said compounds are provided as components of mixtures.

55. The method of claim 54, wherein said mixtures are natural product extracts.

56. The method of claim 48, wherein said effect is a synergistic effect.

57. The method of claim 48, wherein one or both of steps (a) and (c) is carried out using a robotics system.

58. The method of claim 48, wherein one or both of steps (a) and (c) is carried out using microfluidics.

59. The method of claim 48, wherein one or both of steps (a) and (c) is carried out using ink-jet printer technology.

60. A method for screening two-compound or higher order combinations for biological activity, said method comprising the steps of:

(a) creating an array of at least 10,000 unique two-compound or higher order combinations from a set of compounds,

(b) providing living test cells,

(c) contacting said array of combinations of compounds with said test cells under conditions that ensure that each compound combination/test cell contacting is segregated from the others,

(d) detecting or measuring a property of the test cells,

(e) selecting combinations of compounds that cause an effect on said property of the test cells that is different from the effect of each compound of the combination by itself, and

(f) repeating steps (a) through (e) at least twice over a period of ten days or less, wherein, in step (a), said array of at least 10,000 two-compound or higher order combinations is different in two or more repetitions.

61. A method for screening combinations of compounds for biological activity, said method comprising the steps of:

(a) providing living test cells,

(b) contacting said test cells with at least 100 compounds under conditions that ensure that each compound/test cell contacting is segregated from the others,

(c) detecting or measuring a property of said test cells,

(d) selecting compounds that cause a change in said property relative to said property of said test cells not contacted with said compounds,

(e) creating an array of at least 49 unique two-compound or higher order combinations from the identified compounds,

(f) contacting said array of combinations of compounds with test cells under conditions that ensure that each compound combination/test cell contacting is segregated from the others,

(g) detecting or measuring a property of the test cells of step (f), and

(h) selecting combinations of compounds that cause an effect on said property of step (g) that is different from the effect of each compound of the combination by itself.

62. The method of claim 61, wherein the test cells of step (a) are the same as the test cells of step (f).

63. The method of claim 61, wherein the property of step (c) is the same as the property of step (g).

64. The method of claim 1, wherein at least one of said compounds is a small molecule.

65. The method of claim 64, wherein said small molecule is an FDA-approved drug.

66. The method of claim 64, wherein each of said compounds is a small molecule.

67. The method of claim 66, wherein said small molecules are FDA-approved drugs.

68. The method of claim 28, wherein at least one of said compounds is a small molecule.

69. The method of claim 68, wherein said small molecule is an FDA-approved drug.

70. The method of claim 68, wherein each of said compounds is a small molecule.

71. The method of claim 70, wherein said small molecules are FDA-approved drugs.

72. The method of claim 48, wherein at least one of said compounds is a small molecule.

73. The method of claim 72, wherein said small molecule is an FDA-approved drug.

74. The method of claim 72, wherein each of said compounds is a small molecule.

75. The method of claim 74, wherein said small molecules are FDA-approved drugs.

76. The method of claim 48, wherein at least one of said compounds is a small molecule.

77. The method of claim 76, wherein said small molecule is an FDA-approved drug.

78. The method of claim 76, wherein each of said compounds is a small molecule.

79. The method of claim 78, wherein said small molecules are FDA-approved drugs.

80. The method of claim 60, wherein at least one of said compounds is a small molecule.

81. The method of claim 80, wherein said small molecule is an FDA-approved drug.

82. The method of claim 80, wherein each of said compounds is a small molecule.

83. The method of claim 82, wherein said small molecules are FDA-approved drugs.

84. The method of claim 1, wherein said creating step (b) comprises contacting at least seven of said compounds with each other in a pair-wise manner.

85. The method of claim 1, wherein each of said combinations screened for biological activity is a two-compound combination.

86. The method of claim 28, wherein each of said combinations screened for biological activity is a two-compound combination.

87. The method of claim 1, wherein each of said combinations screened for biological activity is a three-compound combination.

88. The method of claim 28, wherein each of said combinations screened for biological activity is a three-compound combination.